Citation:

Furtado JD, Campos H, Appel LJ, Miller ER, Laranjo N, Carey VJ, Sacks FM. Effect of protein, unsaturated fat, and carbohydrate intakes on plasma apolipoprotein B and VLDL and LDL containing apolipoprotein C-III: results from the OmniHeart Trial. *Am J Clin Nutr.* 2008 Jun;87(6):1623-30.

PubMed ID: 18541549

Study Design:

Randomized Crossover Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this research was to study the differences in apo B lipoproteins with and without apo C-III after 3 healthy diets based on the Dietary Approaches to Stop Hypertension Trial diet.

Inclusion Criteria:

- Participants lived in the greater Boston, MA and greater Baltimore, MD areas
- Adult men and women aged ≥ 30 years
- Systolic blood pressure 120-159 mmHg, diastolic blood pressure < 100 mmHg
- Fasting LDL cholesterol <220 mg/dl and TGs < 750 mg/dl

Exclusion Criteria:

Described in another study of the OmniHeart randomized trial.

Description of Study Protocol:

Recruitment

Eligibility was determined during screening visits, at which time a blood sample was taken for baseline measurements.

Design: Randomized crossover trial. Each participant was randomly assigned each of 3 healthy diets for 6 weeks.

Blinding used (if applicable): All laboratory staff were blinded to the diet sequences of the participants.

Intervention (if applicable)

- Each of the three diets (Carb, Unsat, Prot) consisted of commonly available foods.
- Diets differed by emphasis of either carbohydrate, unsaturated fat, or protein
- The initial calorie content was determined for each participant, based on body size, sex, and physical activity level.
- Body weight was monitored daily, and calorie content of the diets was adjusted to maintain initial body weight.
- All meals, snacks, and beverages, except for discretionary calorie-free beverages, were provided to the participants.
- Each diet was maintained for 6 weeks.
- Participants ate their usual free-living diet for a minimum of 2 weeks before beginning the next diet period.

Statistical Analysis

- The primary outcome was apo B concentration in whole plasma and in the lipoprotein subfractions.
- Cholesterol, TG, apo C-III, and apo E concentrations were examined as secondary outcomes.
- The main comparisons in this study were made among the Carb, Unsat, and Prot diets, in particular the Prot-Carb diets and the Unsat-Carb diets; the Unsat-Prot diet was of secondary interest and was mathematically contained in the other 2 differences.
- Paired *t* tests of the between-diet differences were used to assess the differential effects of the diets.
- Secondarily, the change from baseline elicited by each diet with paired *t* tests of the difference between baseline and postdiet samples were made.
- Analyses were performed with the uses of SAS version 9.1.
- The t tests were all two-sided and statistical significance was defined as $P \leq 0.05$.

Data Collection Summary:

Timing of Measurements

Blood sample measurements were made at baseline and at the end of the 4th and 6th week of each diet period.

Dependent Variables

- Primary outcome: apo B concentration in whole plasma and in the lipoprotein subfractions
- Secondary outcome: cholesterol, TG, apo C-III, and apo E concentrations

Independent Variables

- Carb diet: 58% of energy carbohydrate, 27% fat (6% saturated, 13% monounsaturated, and 8% polyunsaturated) and 15% protein (5.5% meat and 9.4% plant and dairy)
- Prot diet: 48% of energy carbohydrate, 27% fat (6% saturated, 13% monounsaturated, 8% polyunsaturated) and 25% protein (9% meat, 15% plant and dairy)
- Unsat diet: 48% of energy carbohydrate, 37% fat (6% saturated, 21% monounsaturated, 10% polyunsaturated) and 15% protein (5.5% meat, 9.5% plant and dairy)
- Participants were requested to maintain their usual intake of alcoholic beverages, not to exceed 2 drinks/d.
- Participants were instructed to eat only the food provided and to maintain their usual levels

of physical activity.

Control Variables

Description of Actual Data Sample:

Initial N: 191 (44% women)

Attrition (final N): 162

Age: 53 ± 10 years

Ethnicity: 55% African American

Other relevant demographics: 74% of women were postmenopausal

Anthropometrics: mean body mass index (kg/m^2): 30.4 ± 6.1

Location: Center for Human Nutrition, Department of Epidemiology and Center for a Livable Future, Department of Environmental Sciences, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Summary of Results:

Key Findings

- Compared with the Carb diet, the Prot diet reduced plasma apo B and triglycerides in VLDL with apo C-III (16%, P = 0.07; 11%, P = 0.05, respectively), and apo B in LDL with apo C-III (16%, P = 0.04).
- Compared with the Unsat diet, the Prot diet reduced triglycerides in VLDL with apo C-III (16%, P = 0.02).
- Compared with baseline (subjects' usual diet was higher in saturated fat), the Prot diet reduced apo B in LDL with apo C-III (11%, P = 0.05).
- All 3 diets reduced plasma total apo B (6 - 10%, P < 0.05) and apo B in the major type of LDL, LDL without apo C-III (8 - 10%, P < 0.01).
- All 3 diets reduced the ratio of apo C-III to apo E in VLDL

Author Conclusion:

Substituting protein for carbohydrate in the context of a healthy dietary pattern reduced atherogenic apo C-III-containing LDL and its precursor, apo C-III-containing VLDL, resulting in the most favorable profile of apo B lipoproteins. In addition, compared with a typical high-saturated fat diet, healthy diets that emphasize carbohydrate, protein, or unsaturated fat reduce plasma total and LDL apo B and produce a lower more metabolically favorable ratio of apo C-III to apo E.

Reviewer Comments:

Relatively large sample size, participants were demographically heterogeneous, strengthening the application to the US population. Authors note the following limitations:

- *Relatively brief duration of each diet period does not allow for assessment of permanence of lipoprotein changes, but the 4 week results were similar to the 6 week results, suggesting that a new baseline had been reached.*
- *Controlled diet design makes it difficult to gauge the success of long-term adherence to each diet when the diet is chosen by people*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes

2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	???
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A

5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes

	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes